Community Acquired Acute Kidney Injury: Findings from a large population cohort

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Abstract

Background. The extent of patient contact with medical services prior to development of community acquired AKI is unknown.

Aims. We examined the relationship between incident community acquired electronic AKI alerts (CA-AKI), previous contact with hospital or primary care and clinical outcomes.

Design. A prospective national cohort study of all electronic AKIalerts representing adult CA-AKI**.**

Methods. Data was collected for all cases of adult (≥18yrs of age) CA-AKI in Wales between 1st November 2013 and 31st January 2017.

Results. There were a total of 50560 incident CA-AKI alerts. In 46.8% there was a measurement of renal function in the 30 days prior to the AKI alert. In this group, in 63.8% this was in a hospital setting, of which 37.6% were as an inpatient and 37.5% in A&E. Progression of AKI to a higher AKI stage (13.1% vs. 9.8%, $p<0.001$) (or for AKI 3 an increase of ≥50% from the creatinine value generating the alert), the proportion of patients admitted to Intensive Care (5.5% vs. 4.9%, $p=0.001$) and 90-day mortality (27.2% vs. 18.5%, $p<0.001$) was significantly higher for patients with a recent test. 90-day mortality was highest for patients with a recent test taken in an inpatient setting prior to CA-AKI (30.9%).

Conclusion. Almost half of all patients presenting with CA-AKI are already known to medical services, the majority of which have had recent measurement of renal function in a hospital setting, suggesting that AKI for at least some of these may potentially be predictable and/or avoidable.

Introduction

Acute kidney injury (AKI) is a common health problem worldwide, affecting up to 1% of the general population and 15% of all hospitalised patients (1-3). Severe AKI requiring dialysis is associated with a high rate of in-hospital mortality (4). Less severe degrees of renal injury have also been associated with a significantly heightened risk of death, prolonged in-patient hospital stay and increased costs (5, 6). AKI may also have long-lasting detrimental effects on a patient's health, with an increased incidence of subsequent Chronic Kidney Disease (CKD) and mortality (7-10).

AKI may occur during hospitalisation (HA-AKI), may be present at the time of admission to hospital or may occur and be managed in the community. To date the majority of published studies contributing to our understanding of epidemiology and outcome of AKI, are based on AKI in hospitalised patients (11-13). Amongst hospitalised patients the incidence of community acquired AKI (CA-AKI) is roughly twice that of hospital acquired AKI (14). In contrast to HA-AKI much less is known regarding the nature and impact of CA-AKI of which 30-40% is not hospitalised (15, 16), AKI within primary care and the interface between primary and secondary care. Up to half of all AKI detected by an electronic AKI alert based on a change in creatinine criteria, is accounted for by CA-AKI (15) of which only 30% is detected in primary care (17). In this manuscript we have examined the relationship between incident electronic CA-AKI alerts and previous contact with either hospital services or primary care and related this to the clinical course/outcome of an AKI episode. Our aim was to highlight potential "predictable" AKI and possible missed opportunities to minimise the risk and impact of AKI.

Methods

Setting: Data was collected across the National Health Service in Wales which serves a population of 3.06 million. The study was approved under "Service Evaluation Project Registration". The previously described (and validated) Welsh electronic AKI reporting system (15, 18), utilises the Welsh Laboratory Information Management System (LIMS) (InterSystems TrakCare Lab) to automatically compare in real time measured creatinine values on an individual patient against previous results, to generate electronic alerts using an nationally agreed algorithm based on KDIGO AKI criteria (Supplementary Figure 1) (19). Three "rules" are applied to generate alerts differing in the time period from which the baseline creatinine is obtained. Rule 1 alerts represent a >26μmol/l increase in SCr within the previous 48 hours and are issued only if rule 2 and rule 3 are not satisfied. Rule 2 alerts represent a ≥50% increase in SCr within the previous 7 days, and a rule 3 alert represents a ≥50% increase in SCr from the median of results from the previous 8 to 365 days.

Data Collection: Data was collected for all cases of adult (≥18yrs of age) CA-AKI in Wales between 1st November 2013 and the 31st January 2017. Clinical location, patient age, AKI stage and the rule under which the AKI alert was generated was collected together with all measurements of renal function for up to 30 days following the AKI alert. To prevent inclusion of known patients receiving renal replacement therapy, alerts transmitted by patients from a renal, renal transplant, or dialysis setting, and by patients who had a previous blood test in a dialysis unit were excluded.

Mortality data were collected from the Welsh Demographic Service (WDS).

Data analysis: CA-AKI was classified as any patients with an e-alert generated in a non-in-patient setting. We defined an incident episode of AKI as 30 days, i.e. any AKI e-alert for the same patient within 30 days of a previous alert was not considered a new episode. The Medical Record Number (MRN) was used as the patient identifier. This is a unique reference number allocated to each patient registered in the National Laboratory Information Management System (LIMS) and allows for multiple visits/blood test requests across all locations in Wales to be linked.

Patients were classified into two groups; those with a measurement of renal function within the preceding 30 days of the incident AKI alert (Recent test), and those without (No recent test). Alerts for the latter group were all therefore generated by a baseline creatinine value derived from the median of results from the last 30 to 365 days.

Progression of AKI was defined as a peak AKI stage higher than that associated with incident e-alert or for stage 3 alerts an increase ≥50% from the Serum Creatinine value (SCr) generating the alert. Critical care admission was also used as a surrogate marker for disease severity, and was defined as a measurement of renal function in an Intensive Care (ICU) setting during the 30 day AKI episode. Pre-existing chronic kidney disease (PeCKD) was defined as an eGFR (calculated by CKDEpi eGFR formula (20)) <60ml/min/1.73m^2 derived from the baseline SCr.

Statistical analysis was carried out using SPSS software, version 20 (SPSS, Inc., Chicago, IL). Student's t test and ANOVA were used for analysis of normally distributed data. Categorical data were compared using a Pearson chi-squared test. P values less than 0.05 were considered statistically significant differences.

Results

Over the study period there were a total of 50560 incident CA-AKI alerts. The demographic data on the cohort is shown in table 1.

CA-AKI and measurement of renal function in preceding 30 days.

Characteristics of patients with a recent measurement of renal function (Recent test) and those without a recent measurement of renal function (No recent test) are shown in table 1. 46.8% (23658) of all CA-AKI had a measurement of renal function during the 30-day period prior to the AKI alert. The cohort of "Recent test" patients at the time of the incident alert, were significantly older (70.3±16.4yrs vs. 68.9±18.5yrs, p<0.001), had a higher proportion of male patients (48.2% vs. 42.8%, p<0.001), a higher proportion of pre-existing CKD (37.9%% vs. 30.9%, p<0.001), and a higher proportion of AKI 1 vs. AKI2/3 (recent test; AKI1 75% vs. no recent test; AKI173.2%, p<0.001).

In this cohort of those with a previous measurement prior to the AKI episode, 63.8% of measurements were taken in a hospital setting (15096 of 23658), of which 37.6% were performed as an in-patient (n=5677, mean time since previous test 10.7±9.6days), 37.5% in an Accident and Emergency (A&E) setting (n=5667, mean time since previous test 7.3±8.8 days) and 16.6% in an outpatient setting (n=2512, mean time since previous test 13.5±9.6 days). Only 30.8% of tests prior to the AKI episode in the "recent test" cohort were performed in primary care (7285 of 23658). The mean time since the previous result in primary care was 13.3±9.7 days.

Pre-existing CKD prior to the AKI episode was highest in those with previous test results generated in primary care (46.9%) followed by patients with a result generated in A&E **(33.6%)** and patients with a test of renal function in an in-patient setting (31.5%, p<0.001 for all comparisons). In contrast the highest proportion of AKI1 was seen in patients previously monitored in A&E (78.8%) followed by primary care (75.5%) and an in-patient setting (73.2%, P<0.001 for all comparisons).

Clinical setting of AKI detection

The clinical location of AKI alerts is shown in Table 3. For the cohort of patients with no recent test a higher proportion of AKI was detected in primary care (38.4% vs. 23.5%, P<0.001) and less at A&E (48.3% vs. 55.7%, p<0.001), than those with a recent test.

Within the recent test cohort, an A&E presentation with the incident AKI episode was significantly more likely for patients with previous A&E testing prior to the AKI alert (81.0%) compared to previous in-patient testing prior to the AKI alert (60.2%, p<0001) which was significantly greater than for primary care tested patients (47.9%, p<0.001).

In contrast presentation to primary care with the incident AKI episode was significantly greater for patients with previous primary care testing (43.2%) compared to previous in-

patient testing (19.2%, p<0.001), which was significantly greater than for patients previously tested at A&E (10.3%, p<0.001).

Response to and Impact of AKI

The clinical location of the blood test immediately following the AKI alert is shown in Table 4. Patients who did not have a test result in the 30 days prior to the incident AKI alert were less likely to have a repeat blood test after the incident AKI alert than those known to medical services previously (81.0% vs. 88.9%, p<0.001). For those who did have a repeat blood test following the incident AKI episode the time to repeat was significantly shorter for the known cohort (known 6.4±12.0days vs. 10.2±17.3days p<0.001), this relationship was consistent for the groups in which the repeat blood test was undertaken in Primary care (known 12.4±14.2days vs. 17.6±19.3days p<0.001), A&E (known 6.4±12.3days vs. 7.5±16.5days p<0.001) or in an in-patient setting (known 2.3±5.5days vs. 3.1±8.3days, p<0.001).

A higher proportion of those not known, following the incident AKI episode remain in primary care for subsequent blood tests (24.2% vs. 16.5%, p<0.001), and a lower proportion are admitted as an in-patient to hospital (29.9% vs. 36.1%, p<0.001) than those who were known to medical services.

In the patients with a blood test prior to the AKI alert either in A&E or in an in-patient setting a higher proportion were likely to be seen in hospital (either at A&E or as an in-patient) for retesting of renal function following an AKI alert than those in whose previous measurement of renal function was undertaken in primary care (69.2% vs. 50.1% p<0.001), in which a higher proportion had renal function re-measured in primary care following the alert (30.2% vs. 10.4%, p<0.001).

Overall 90-day mortality for CA-AKI was 22.6%. Progression of AKI to a higher AKI stage (or for AKI 3 an increase ≥50% from the SCr generating the alert) was greater in the cohort of patients previously known to medical services (13.1% vs. 9.8%, p<0.001). The proportion of patient admitted to Intensive Care was also higher in this group (5.5% vs. 4.9%, p=0.001). In addition 90-day mortality was also significantly higher for patients already “known” to medical services compared to those with no blood test in the 30-days prior to the AKI alert (27.2% vs. 18.5%, p<0.001). In the cohort of “known” patients at the time of the incident alert (i.e. a blood test within 30 days), mortality was higher in those seen prior to the AKI episode as an in-patient (30.9%) than either those seen prior in Primary care (26.9%, p<0.001 vs. in-patient) or seen previously at A&E (26.8%, p<0.001 vs. in-patient).

Discussion

Despite advances in health care, the incidence of AKI is increasing both in the UK (21, 22) and USA (23, 24). Potential explanations for this increase may be related to increasingly aggressive medical and surgical therapies in a largely aging population with multiple comorbid conditions (25). The significance of AKI is highlighted by the increase in mortality associated with even small changes in serum creatinine (26-28). In contrast to HA-AKI less is known regarding CA-AKI although it is clear that CA-AKI is a major contributor to the overall disease burden (13, 29). In this manuscript we provide a novel insight into the nature and outcome of CA-AKI and the patient journey in the days and weeks prior to and immediately following the detection of AKI.

The first notable finding in this study is that almost half of the patients who generated a CA-AKI alert have a measurement of renal function in the 30 days preceding the alert. For the majority of these patients this measurement was undertaken within two weeks of the incident AKI episode. As might be expected this group was older and had a higher proportion of CKD suggesting that this is a group with higher co-morbidity and therefore AKI risk factors. In keeping with this, mortality was also higher in patients which were known to medical services prior to development of AKI, at least as judged by a recent test of renal function. Of those with a recent test, for more than half, the review and measurement of renal function had been undertaken in a hospital setting. Although labelled as CA-AKI, given the short time frame between test and AKI incident alert it is possible that the incident AKI episode was related to either the illness precipitating the consultation or change made in response to the presenting symptoms. It is interesting therefore to speculate that within this group that AKI is some cases at least was predictable and therefore potentially avoidable. Within the group with a "recent test" the highest mortality was seen in patients who had a measurement of renal function in an inpatient setting within roughly a fortnight of the AKI episode. This was also the group with the highest incidence of de-novo AKI (i.e. the lowest proportion of pre-existing CKD). The lower mortality in patients monitored in primary care prior to the AKI episode reflects the highest proportion of acute on chronic AKI, whilst the lower mortality in those with a measurement of renal function at A&E prior to the AKI episode reflect less severe AKI at presentation which may also reflect the shortest time interval between the previous measured renal function and the AKI episode suggesting early presentation.

Whilst this study highlights a large cohort of patients who develop AKI following recent hospital attendance, a weakness is its dependence of an e-alert system which lacks clinical context. Further work is therefore required to understand the relationship between medical service interactions/interventions, patient inter-current illness and their contribution to the development of CA-AKI, to identify any intervention or patient related risk factors which in particular might highlight who among the recent hospital attendees might be at risk and potentially benefit from early clinical review. Recent data however, derived from a cohort of patients with HA-AKI have identified five clusters of diagnoses to be associated with development of AKI: sepsis, heart disease, poly-trauma, liver disease and cardiovascular surgery (30). This suggests that patients recently discharged back to the community following hospital attendance for these indications may benefit from early clinical review to facilitate early detection, prompt re-assessment of patients, close monitoring of patient physiology, review of medication or consideration of hospitalisation in an attempt to improve patient outcomes.

Whilst presentation to A&E is the most common presentation for CA-AKI, for those without a recent test the likelihood of presentation to primary care with the incident episode of AKI was higher. For patients in whom renal function was recently measured the site of presentation with the incident AKI episode also reflected where the previous blood test was undertaken, such that a previous recent blood test in A&E predicted presentation to A&E with the incident AKI episode and similarly a recent blood test in primary care predicted those who presented to primary care with the AKI episode. This suggests that patients when acutely unwell are most likely to return to a "familiar" port of call for health advice. Our data also suggest that patients who have had recent measurement of renal function are more likely to have a repeat measurement following an AKI alert and that the time to a repeat blood test for this group is also significantly shorter. It is likely that this reflects both patient as well as medical staff related behavioural factors. The place of detection of AKI also influences the likelihood of hospital admission with AKI detected in primary care generating the lowest number of admissions. This is consistent with our previous data on AKI in primary care which demonstrated that admission from primary care was associated with AKI severity (17). Whilst admission was associated with higher mortality it was of note that in surviving patients non-admission was associated with worse renal outcomes, and that patients who were not hospitalized had a lower rate of renal recovery and a greater likelihood of developing an eGFR <60ml/min/1.73m^2 for the first time, which may be indicative of

development of *de novo* CKD (15). This is also consistent with the recent report of Sawheny in which non-admitted AKI whilst having a lower mortality was associated with greater non-recovery of renal function (31). Previous data suggest that "non-admission" is at least in part is due to lack of recognition of the significance of the alert (14-16). Furthermore, we have demonstrated that a delayed response to the alert in primary care is associated with a significantly worse renal outcome (17). Based on these observations we have previously recommended that a clinical review or referral together with a repeat measurement of renal function within 7 days should be considered an appropriate response to AKI e-alerts in primary care.

In conclusion this study demonstrates that almost half of all patients presenting with CA-AKI are already known to medical services, suggesting that AKI for at least some of these may be potentially predictable and/or avoidable. Of these almost two thirds have a recent interaction with hospital either as an inpatient or via an A&E visit, thus suggesting that a sizable proportion of what is currently labelled as community acquired AKI may in fact relate to recent "hospitalisation" and may not actually be "community acquired". The challenge is to identify the group of patients in whom AKI may be predictable and for whom early clinical review is likely to reduce the incidence of or alter the outcome following AKI.

Acknowledgements

The work was carried out under the auspices of the Welsh AKI steering group which is sponsored by the Welsh Renal Clinical Network and Welsh Government

Disclosures; There are no competing interests

Supplementary Figure Legend

Supplementary Figure 1: Algorithm for generating e-alerts for Acute Kidney Injury based on serum creatinine (SCr) changes with time. RV, Reference value, defined as the SCr value with which the index SCr value is compared; D, difference between current and lowest previous result within 48 hours; RI, Population reference interval.

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Table 1: Comparison of CA-AKI patients with a measurement of renal function within the preceding 30 days of an alert (Recent test) vs. those without a measurement of renal function within the preceding 30 days of an alert (No recent test)

Variable	All CA-AKI	No recent test	Recent test	P value (Recent test vs. No recent test)	'Recent test' cohort			
					Previous test in primary care (PC)	Previous test as an inpatient (IP)	Previous test at A&E (AE)	P value ('Recent test' groups)
Number of episodes	50560	26902	23658		7285	5677	5667	
Mean age ±SD (yrs)	69.6 ±17.6	68.9 ±18.5	70.3 ±16.4	P<0.001	74.1 ±14.1	69.8 ±16.9	69.8 ±17.4	P<0.001
Males, n (%)	22933 (45.4)	11527 (42.8)	11406 (48.2)	P<0.001	3337 (45.8)*	2818 (49.6)	2748 (48.5)	*P=0.002 vs. AE&IP
Pre existing CKD, n (%)	17212 (34.2)	8303 (30.9)	8909 (37.9)	P<0.001	3405 (46.9)	1766 (31.2)	1904 (33.6)	P<0.001 for all
AKI stage 1, n (%)	37424 (74.0)	19686 (73.2)	17738 (75.0)	P<0.001 AKI1 vs. AKI2/3	5499 (75.5) *#	4157 (73.2)#	4468 (78.8)	AKI1 vs. AKI2/3 *P=0.003 vs. IP #P<0.001 vs. AE
AKI stage 2, n (%)	8020 (15.9)	4429 (16.5)	3591 (15.2)		1113 (15.3)	980 (17.3)	807 (14.2)	
AKI stage 3, n (%)	5116 (10.1)	2787 (10.4)	2329 (9.8)		673 (9.2)	540 (9.5)	392 (6.9)	
Admission to ICU, n (%)	2600 (5.1)	1308 (4.9)	1292 (5.5)	P=0.002	337 (4.6)	384 (6.8)	341 (6.0)	n/s
Progression of AKI, n (%)	5734 (11.3)	2633 (9.8)	3101 (13.1)	P<0.001	986 (13.5)*	756 (13.3)*	678 (12.0)	P=0.02 vs. A&E
90 day mortality, n (%)	11285 (22.6)	4947 (18.5)	6338 (27.2)	P<0.001	1953 (26.9)	1744 (30.9)*	1505 (26.8)	*P<0.001

Baseline eGFR data were missing for 198 episodes (69, No recent test; 129, Recent test; 18, PC; 8, IP; 5, A&E) and excluded from analysis of the Pre-existing CKD variable. Mortality data was available for 50022 episodes (26715, No recent test; 23307, Recent test; 7262, PC; 5643, IP; 5609, A&E). CA-AKI, Community acquired AKI; PeCKD, Pre-existing chronic kidney disease; ICU, Intensive Care Unit; PC, Primary Care; IP, Inpatient; A&E, Accident and Emergency.

Table 2: Clinical location of blood test taken prior to and within 30 days of incident AKI episode.

Clinical location of previous test	Number of CA-AKI episodes	% of all CA-AKI episodes	Mean time from previous test to AKI episode ±SD (days)
No recent test	26902	53.2	-
GP Practice	7285	14.4	13.3 ±9.7
Inpatient	5677	11.2	10.7 ±9.6
Accident & Emergency	5667	11.2	7.3 ±8.8
Out Patient	2512	5.0	13.5 ±9.6
Day Case	1240	2.5	10.4 ±8.6
Other*	1099	2.2	9.6 ±9.7
Private Patient	98	0.2	8.2 ±8.1
Research and Development	42	0.1	6.9 ±8.0
Ante-natal	38	0.1	14.2 ±11.0
Total	**26902**	**100.0**	**10.9 ±9.7**

**Other included the following patient types: Other, Renal, Renal and Transplant, Renal Dialysis, Community, Genito-Urinary Medicine, Family Planning, Environmental, Home Office, and Occupational Health.*

Table 3: Clinical location of AKI alert.

Clinical location of AKI alert, n (%)	All CA-AKI	No recent test	Recent test	P value (Recent test vs. No recent test)	'Recent test' cohort			
					Previous test in primary care	Previous test as an inpatient	Previous test at A&E	P value ('Recent test' groups)
Accident & Emergency	26149 (51.7)	12980 (48.3)	13169 (55.7)	P<0.001	**3488 (26.5)**	**3417 (25.9)**	**4592 (34.9)**	P<0.001 for all
GP Practice	15905 (31.5)	10334 (38.4)	5571 (23.6)	P<0.001	**3144 (56.4)**	**1092 (19.6)**	**583 (10.5)**	P<0.001 for all
Out Patient	5224 (10.3)	2729 (10.1)	2495 (10.6)	n/s	**439 (17.6)**	**617 (24.7)**	**255 (10.2)**	P<0.001 for all
Day Case	1716 (3.4)	342 (1.3)	1374 (5.8)	P<0.001	**100 (7.3)**	**290 (21.1)**	**123 (9.0)**	P<0.001 for all
Other*	1306 (2.6)	437 (1.6)	869 (3.7)	-	**107 (12.3)**	**228 (26.2)**	**100 (11.5)**	-
Private Patient	148 (0.3)	47 (0.8)	101 (0.4)	P<0.001	**3 (3.0)**	**23 (22.8)**	**6 (5.9)**	-
Ante-natal	68 (0.1)	21 (0.1)	47 (0.2)	P<0.001	**3 (6.4)**	**7 (14.9)**	**1 (2.1)**	-
Research and Development	44 (0.1)	12 (0.04)	32 (0.1)	P<0.001	**1 (3.1)**	**3 (9.4)**	**7 (21.9)**	-
Total	**50560**	**26902**	**23658**	**-**	**7285**	**5677**	**5667**	**-**

**Other included the following patient types: Other, Renal, Renal and Transplant, Renal Dialysis, Community, Genito-Urinary Medicine, Family Planning, Environmental, Home Office, and Occupational Health.*

Table 4: Clinical location of blood test following the incident AKI alert.

Clinical location of repeat test, n (%) mean time to repeat test ±SD (days)	All CA-AKI	No recent test	Recent test	P value (Recent test vs. No recent test)	'Recent test' cohort		
					Previous test in primary care	Previous test as an inpatient or at A&E	P value ('Recent test' groups)
Inpatient	16579 (32.8)	8032 (29.9)	8547 (36.1)	P<0.001	**2309 (27.0)**	**4905 (57.4)**	P<0.001
	2.7 ±7.1	3.1 ±8.3	2.3 ±5.7	P<0.001	**2.2 ±5.5**	**2.2 ±5.5**	n/s
GP Practice	10396 (20.6)	6503 (24.2)	3893 (16.5)	P<0.001	**2199 (56.5)**	**1182 (30.4)**	P<0.001
	15.9 ±18.1	17.6 ±19.3	13.1 ±15.5	P<0.001	**12.4 ±14.2**	**13.9 ±17.4**	P=0.007
Accident & Emergency	9998 (19.8)	4955 (18.4)	5043 (21.3)	P<0.001	**1408 (27.9)**	**2947 (58.4)**	P<0.001
	6.4 ±14.3	7.5 ±16.5	5.4 ±11.8	P<0.001	**4.3 ±11.5**	**6.0 ±12.1**	P<0.001
No repeat test	7923 (15.7)	5306 (19.7)	2617 (11.1)	P<0.001	**853 (32.6)**	**1348 (51.5)**	n/s
	-	-	-	-	**-**	**-**	-
Out Patient	2788 (5.5)	1245 (4.6)	1543 (6.5)	P<0.001	**266 (17.2)**	**470 (30.5)**	n/s
	19.7 ±21.2	26.8 ±23.7	14.0 ±16.9	P<0.001	**21.3 ±21.9**	**13.1 ±17.6**	P<0.001
Other*	1431 (2.8)	522 (1.9)	909 (3.8)	P<0.001	**169 (18.6)**	**211 (23.2)**	-
	9.8 ±15.9	12.8 ±19.4	8.1 ±13.2	P<0.001	**7.6 ±13.7**	**6.2 ±12.3**	n/s
Day Case	1291 (2.6)	288 (1.1)	1003 (4.2)	P<0.001	**76 (7.6)**	**260 (25.9)**	P<0.001
	9.6 ±12.4	15.2 ±17.3	8.1 ±10.1	P<0.001	**7.6 ±11.0**	**7.6 ±13.0**	n/s
Private Patient	87 (0.2)	33 (0.1)	54 (0.2)	P<0.001	**2 (3.7)**	**7 (13.0)**	n/s
	7.9 ±15.7	12.8 ±19.9	5.1 ±12.1	P=0.034	**10.4 ±14.7**	**5.7 ±8.0**	n/s
Research and Development	37 (0.1)	7 (0.03)	30 (0.1)	P<0.001	**-**	**6 (20.0)**	-
	3.4 ±8.6	8.6 ±18.2	2.3 ±4.1	n/s	**-**	**2.0 ±2.8**	-
Ante-natal	30 (0.1)	11 (0.04)	19 (0.1)	P<0.001	**3 (15.8)**	**8 (42.1)**	n/s
	8.9 ±16.2	17.3 ±25.0	4.1 ±3.2	P=0.030	**3.5 ±2.0**	**4.5 ±3.8**	n/s
Total	**50560**	**26902**	**23658**	**-**	**7285**	**11344**	**-**
	8.3 ±15.0	**10.2 ±17.3**	**6.4 ±12.0**	**P<0.001**	**7.1 ±12.7**	**5.4 ±11.5**	**P<0.001**

**Other included the following patient types: Other, Renal, Renal and Transplant, Renal Dialysis, Community, Genito-Urinary Medicine, Family Planning, Environmental, Home Office, and Occupational Health.*

SUPPLEMENTARY FIGURE 1